content as directed in the individual section.

[39 FR 18944, May 30, 1974, as amended at 40 FR 22251, Apr. 22, 1975; 40 FR 23725, June 2, 1975; 40 FR 57797, Dec. 12, 1975; 46 FR 2981, Jan. 13, 1981]

§ 436.214 Heat stability.

Store an accurately weighed portion of the sample of approximately 30 milligrams in an unstoppered 50-milliliter Erlenmeyer flask for 4 days in an electric oven at 100° C±1° C. At the end of this period, remove the flask from the oven and allow to cool in a desiccator. Accurately weigh an unheated portion of the original sample of approximately 30 milligrams. Assay both the heated and unheated samples for potency as directed in § 436.204 or § 436.205 of this chapter. Determine the percent loss from the difference in potency between the unheated original sample and the heat-treated sample.

[42 FR 59856, Nov. 22, 1977]

§ 436.215 Dissolution test.

(a) *Equipment.* Use either Apparatus 1 or 2 as described in the United States Pharmacopeia XXI dissolution test.

(b) *Procedure.* For each dosage form listed in the table in this paragraph select the appropriate dissolution medium, rotation rate, sampling time, and apparatus, and proceed as set forth in either Apparatus 1 or 2 methodology of the United States Pharmacopeia XXI dissolution test. Determine the amount of drug substance dissolved by performing the assay described in paragraph (c) of this section. The amount of dissolution medium removed for sampling purposes may be disregarded if the amount removed is not more than 15 milliliters. If more than 15 milliliters is removed, then correct for the volume removed.

Dosage form	Dissolution medium	Rotation rate [1]	Sampling time(s)	Apparatus
Amoxicillin trihydrate and clavulanate potassium chewable tablets..	900 mL distilled water	75	30 min	2
Amoxicillin trihydrate and clavulanate potassium tablets.	.....do	75	.....do	2
Azithromycin capsules.	900 mL 0.10 *M* sodium phosphate buffer, pH 6.0, 0.1 mg/mL trypsin.	100	45 min	2
Bacampicillin hydrochloride tablets.	.....do	75	.....do	2
Cefadroxil hemihydrate capsules.	900 mL distilled water	100	45 min	1
Cefadroxil hemihydrate tablets.	900 mL distilled water	50	30 min	2
Cefixime tablets	900 mL 0.05 *M* potassium phosphate buffer, pH 7.2.	100	45 min	1
Cefpodoxime proxetil tablets	900 mL pH 3.0 glycine buffer	75	30 min	2
Cefprozil tablets.	900 mL purified water	100	45 min	1
Cefuroxime axetil for oral suspension	900 mL Sorenson's Modified Phosphate Buffer, pH 7.0.	50	30 min	2
Cefuroxime axetil tablets.	900 mL 0.07*N* hydrochloric acid	55	15 min. and 45 min	2
Cephalexin hydrochloride monohydrate tablets..	900 mL distilled water	150	45 min	1
Cephradine dihydrate capsules.	900 mL 0.12*N* hydrochloric acid	75	60 min.	2
Clarithromycin tablets.	900 mL 0.10 *M* sodium acetate buffer, pH 5.0.	50	30 min.	2
Doxycycline hyclate tablets.	900 mL distilled water	75	60 min and 90 min	2
Doxycycline monohydrate hydrochloric acid capsules..	900 mL 0.1*N* hydrochloric acid.	75	60 min	2
Erythromycin particles in tablets	900 mL 0.05*M* potassium phosphate buffer, pH 6.8.	75	45 min.	2
Loracarbef capsules.	900 mL distilled water.	50	30 min	2
Oxytetracycline hydrochloride capsules..	900 mL distilled water	75	30 min and 60 min	2
Rifabutin capsules	900 mL 0.01 *N* hydrochloric acid	100	45 min	1
Tetracycline hydrochloride capsules (except 500-mg)..	.....do	75	.....do	2
Tetracycline hydrochloride capsules (500-mg)..	.....do	75	30 min, 60 min, and 90 min	2
Tetracycline hydrochloride tablets.	.....do	75	30 min and 60 min	2
Vancomycin hydrochloride capsules.	900 mL distilled water.	100	45 min	1

[1] Rotation rate of basket or paddle stirring element (revolutions per minute).

(c) *Antibiotic drug content*—(1) *Tetracycline hydrochloride*—(i) *Preparation of working standard solution.* Accurately weigh 20 to 30 milligrams of tetracycline hydrochloride working standard into a suitable-sized volumetric flask. Dissolve and dilute to volume with water. Further dilute an accurately measured portion with distilled water to obtain a known concentration of 0.01 to 0.02 milligram of tetracycline hydrochloride per milliliter.

(ii) *Preparation of sample solutions.* Dilute an accurately measured portion of the sample with sufficient distilled water to obtain a concentration of 0.01 to 0.02 milligram of tetracycline hydrochloride per milliliter (estimated).

(iii) *Procedure.* Using a suitable spectrophotometer and water as the blank, determine the absorbance of each standard and sample solution at the absorbance peak at approximately 276 nanometers. Determine the exact position of the absorption peak for the particular instrument used.

(iv) *Calculation.* Determine the total amount of tetracycline hydrochloride dissolved as follows:

$$T = \frac{A_u \times c \times d \times 900^*}{A_s}$$

where:

T=Total milligrams of drug dissolved;
A_u=Absorbance of sample;
c=Concentration of standard in milligrams;
d=Dilution factor of sample filtrate;
A_s=Absorbance of standard.

*If more than 15 mL of dissolution medium is removed, correct for the volume removed.

(2) *Oxytetracycline hydrochloride; preparation of working standard-solution.* (i) Accurately weigh 30 milligrams of oxytetracycline-base working standard into a suitable-sized volumetric flask. Add 5 milliliters of 0.1*N* hydrochloric acid and swirl the flask to dissolve oxytetracycline base. Dilute an accurately measured portion with distilled water to obtain a known concentration of 0.01 to 0.02 milligram of oxytetracycline per milliliter.

(ii) Proceed as directed in paragraphs (c)(1) (ii), (iii), and (iv) of this section except measure the absorbance at the absorption peak at approximately 273 nanometers.

(3) *Doxycycline hyclate.* Proceed as directed in paragraph (c)(1) of this section, except use the doxycycline working standard.

(4) *Bacampicillin hydrochloride.* Use the ampicillin working standard as the standard of comparison and assay for ampicillin content by either of the following methods.

(i) *Iodometric assay.* Proceed as directed in §436.204 of this chapter, except dilute the working standard to a final concentration of 0.3 milligram of ampicillin per milliliter and use the sample solution as it is removed from the dissolution vessel without further dilution.

(ii) *Hydroxylamine colorimetric assay.* Proceed as directed in §442.40(b)(1)(ii) of this chapter, except:

(*a*) *Buffer.* In lieu of the buffer described in §442.40(b)(1)(ii)(*b*)(*2*) of this chapter, use the buffer prepared as follows: Dissolve 200 grams of primary standard tris (hydroxymethyl) aminomethane in sufficient distilled water to make 1 liter. Filter before use.

(*b*) *Preparation of the working standard solution.* Dissolve and dilute an accurately weighed portion of the ampicillin working standard with sufficient distilled water to obtain a final concentration of 0.3 milligram of ampicillin per milliliter;

(*c*) *Sample solution.* Use the sample solution as it is removed from the dissolution vessel without further dilution; and

(*d*) *Calculations.* Determine the total amount of ampicillin dissolved as follows:

$$T = \frac{(A_u)(c)(d)(900^*)}{A_s}$$

where:

T=Total milligrams of ampicillin equivalent dissolved;
A_u=Absorbance of sample;
c=Concentration of working standard solution in milligrams per milliliter;
d=Dilution factor of sample filtrate;
A_s=Absorbance of standard.

*If more than 15 mL of dissolution medium is removed, correct for the volume removed.

(5) *Cephradine dihydrate*—(i) *Preparation of working standard solution.* Accurately weigh approximately 40 milligrams of cephradine working standard

into a suitable-sized volumetric flask. Dissolve and dilute to volume with 0.12*N* hydrochloric acid. Further dilute with a buffer solution (prepared by dissolving 27.2 grams of sodium acetate trihydrate in a mixture of 12 milliliters of glacial acetic acid and sufficient distilled water to make 2 liters) to obtain a known concentration of 0.01 to 0.03 milligram of cephradine per milliliter.

(ii) *Preparation of sample solution.* Filter the sample and dilute an accurately measured portion of the filtrate with sufficient buffer solution, described in paragraph (c)(5)(i) of this section, to obtain a concentration of 0.01 to 0.03 milligram of cephradine per milliliter (estimated).

(iii) Proceed as directed in paragraphs (c)(1) (iii) and (iv) of this section, except measure the absorbance at the absorption peak at approximately 262 nanometers.

(6) *Amoxicillin trihydrate.* Assay for the amoxicillin content as described in § 440.103d of this chapter, except use the sample as it is removed from the dissolution vessel.

(7) *Vancomycin hydrochloride.* Assay for the vancomycin content as described in § 436.105 of this chapter, except use the sample as it is removed from the dissolution test.

(8) *Erythromycin*—(i) *Preparation of working standard solution.* Accurately weigh approximately 140 milligrams of erythromycin working standard into a 250-milliliter volumetric flask and dissolve in 10 milliliters of methyl alcohol. Add water nearly to volume, mix, and allow the solution to cool. Dilute to volume with water and mix. On the day of use, dilute an accurately measured aliquot with water to obtain a known concentration of 0.28 milligram of erythromycin per milliliter (before adjusting for standard potency).

(ii) *Preparation of sample solution.* Dilute an accurately measured portion of the filtered sample with sufficient 0.05*M* potassium phosphate buffer, pH 6.8, to obtain a concentration of about 0.28 milligram of erythromycin per milliliter (estimated).

(iii) *Procedure.* Transfer 5.0-milliliter aliquots of the working standard solution and sample solution to 25-milliliter volumetric flasks and treat as follows: Add 2.0 milliliters of water, allow to stand for 5 minutes with intermittent swirling. Add 15.0 milliliters of 0.25*N* sodium hydroxide, dilute to volume with sufficient 0.05*M* potassium phosphate buffer, pH 6.8, and mix. Heat to 60 °C for 5 minutes and allow to cool. Using a suitable spectrophotometer and a blank (prepared as per the procedure above except that 2.0 milliliters of 0.5N sulfuric acid is substituted for the 2.0 milliliters of water) for each solution, determine the absorbance of each working standard and sample solution at the absorbance peak at approximately 236 nanometers. Determine the exact position of the absorption peak for the particular instrument used.

(iv) *Calculation.* Proceed as directed in paragraph (c)(1)(iv) of this section.

(9) *Cefuroxime axetil tablets and powder for oral suspension*—(i) *Preparation of working standard solution*—(*a*) *Cefuroxime axetil tablets.* Accurately weigh approximately 60 milligrams of cefuroxime axetil working standard into a suitable-sized volumetric flask. Dissolve in 5 milliliters of methanol and dilute to volume with 0.07*N* hydrochloric acid to obtain a known concentration equivalent to 0.01 to 0.02 milligram of cefuroxime activity per milliliter.

(*b*) *Cefuroxime axetil for oral suspension.* Accurately weigh approximately 15 milligrams of cefuroxime axetil working standard into a 100-milliliter volumetric flask. Dissolve in 5 milliliters of methanol and dilute to volume with Sorenson's Modified Phosphate Buffer, pH 7.0 (4.2 grams of sodium dihydrogen orthophosphate dihydrate and 14.3 grams of hydrogen disodium orthophosphate dodecahydrate per liter of water).

(ii) *Preparation of sample solution*—(*a*) *Cefuroxime axetil tablets.* Filter through a 0.45-micron filter and dilute an accurately measured portion of the filtrate with sufficient 0.07*N* hydrochloric acid to obtain a concentration equivalent to 0.01 to 0.02 milligram of cefuroxime activity per milliliter (estimated).

(*b*) *Cefuroxime axetil for oral suspension.* Filter the sample through an 8-micron filter. A coarse prefilter may be used to prevent clogging. Use the filtrate solution without further dilution.

(iii) *Procedure*—(*a*) *Cefuroxime axetil tablets.* Using a suitable spectrophotometer and 0.07*N* hydrochloric acid as the blank, determine the absorbance of each standard and sample solution at the absorbance peak at approximately 280 nanometers. Determine the exact position of the absorption peak for the particular instrument used.

(*b*) *Cefuroxime axetil for oral suspension.* Using a suitable spectrophotometer and Sorenson's Modified Phosphate Buffer, pH 7.0 (4.2 grams of sodium dihydrogen orthophosphate dihydrate and 14.3 grams of hydrogen disodium orthophosphate dodecahydrate per liter of water) as the blank, determine the absorbance of each standard and sample solution at the absorbance peak at approximately 280 nanometers. Determine the exact position of the absorption peak for the particular instrument used.

(iv) *Calculations.* Determine the total amount of cefuroxime activity dissolved as follows:

$$T = \frac{A_u \times c \times d \times 900}{A_s}$$

where:

T = Total milligrams of cefuroxime activity dissolved;

A_U = Absorbance of sample;

c = Cefuroxime activity of working standard solution in milligrams per milliliter;

d = Dilution factor of sample filtrate; and

A_s = Absorbance of standard.

(10) *Cefixime*—(i) *Preparation of working standard solution.* Accurately weigh approximately 25 milligrams of cefixime working standard into a 500-milliliter volumetic flask. Wet the powder with 0.5 milliliters of methanol, and dilute to volume with 0.05 *M* potassium phosphate buffer, pH 7.2 (prepared by dissolving 6.8 grams of monobasic potassium phosphate in distilled water to a volume of one liter. The pH is adjusted to 7.2 with 1.0*N* NaOH). Sonicate to assure dissolution and mix.

(ii) *Preparation of sample solution.* Forty-five minutes after the beginning of the rotation, withdraw and filter a portion of the solution. For the 400-milligram tablets, pipet 10.0 milliliters of the filtered sample solution into a 100-milliliter volumetric flask. For the 200-milligram tablets, pipet 10.0 milliliters of the filtered sample into a 50-milliliter volumetric flask. Dilute to volume with 0.05 *M* postassium phosphate buffer, pH 7.2.

(iii) *Procedure.* Proceed as directed in paragraphs (c)(1) (iii) and (iv) of this section, except measure the absorbance of the peak at approximately 320 nanometers using 0.05 *M* potassium phosphate buffer, pH 7.2 as the blank.

(11) *Cephalexin hydrochloride monohydrate.* Assay for cephalexin activity of the cephalexin hydrochloride monohydrate as directed in § 442.28 of this chapter, and use U.S.P. dissolution apparatus 1 (10 mesh basket). Use the sample as it is removed from the dissolution vessel.

(12) *Doxycycline monohydrate.* Proceed as directed in paragraph (c)(1) of this section, except use the doxycycline standard.

(13) *Clarithromycin.* Proceed as directed in § 452.50(b)(1) of this chapter except:

(i) *Dissolution medium.* Instead of the mobile phase described in § 452.50(b)(1)(i) of this chapter, use 0.10 *M* sodium acetate buffer prepared as follows: Weigh 13.6 grams of sodium acetate trihyrate into a container sufficient to hold 1 liter of solution. Dissolve the salt in 750 milliliters of distilled water. Adjust the pH of the solution to 5.0±0.05 with glacial acetic acid. Dilute to 1,000 milliliters with distilled water.

(ii) *Preparation of the standard and sample solutions*—(*a*) *Standard solution.* Dissolve (with shaking or sonication) an accurately weighed portion of the clarithromycin working standard, in sufficient methanol to obtain a solution having a known concentration of approximately 625 micrograms per milliliter of clarithromycin. Quantitatively transfer and dilute an aliquot of this solution with mobile phase (described in § 452.50(b)(1)(i) of this chapter) and mix to obtain a solution of known concentration of approximately 125 micrograms per milliliter of clarithromycin.

(*b*) *Sample solution.* Use the sample solution as it is removed from the dissolution vessel after diluting and mixing with mobile phase (described in § 452.50(b)(1)(i) of this chapter) 1:2 for

the 250-milligram tablet and 1:4 for the 500-milligram tablet.

(*c*) *Calculations.* Determine the total amount of clarithromycin activity dissolved as follows:

$$T = \frac{A_U \times c \times d \times 900}{A_s}$$

where:

T = Total milligrams of clarithromycin activity dissolved;

A_U = Area of the clarithromycin peak (at a retention time equal to that observed for the standard) in the chromatogram of the sample;

A_S = Area of the clarithromycin peak in the chromatogram of the clarithromycin standard;

c = Clarithromycin activity in the clarithromycin working standard solution in milligrams per milliliter; and

d = Dilution factor of sample filtrate.

(14) *Azithromycin.* Proceed as directed in § 452.60(b)(1) of this chapter, except:

(i) *Dissolution medium.* Dissolve 85.2 grams of sodium phosphate dibasic and dilute to volume with ultrapure deionized or high-performance liquid chromatographic-grade water in a stoppered 2-liter graduated cylinder. Dilute this entire solution in an appropriate, suitably sized container with 4 liters of ultrapure deionized or high-performance liquid chromatographic-grade water. Adjust the pH to 6.0±0.05 with concentrated hydrochloric acid (about 40.5 milliliters). Add 600 milligrams of trypsin and mix well.

(ii) *Preparation of the standard and sample solutions*—(*a*) *Standard solution.* Accurately weigh approximately 15 milligrams of the azithromycin working standard into a 50-milliliter volumetric flask. Add 25 milliliters of the dissolution medium and sonicate briefly. Dilute to volume with dissolution medium and mix well. Pipet 2.0 milliliters of this solution into a 25-milliliter volumetric flask and dilute to volume with the mobile phase described in § 452.60(b)(1)(i) of this chapter. Pipet 4.0 milliliters of this solution into a 25-milliliter volumetric flask and bring to volume with the mobile phase.

(*b*) *Sample solution.* Filter the sample solutions through a 0.45-micron filter before use. Pipet 2.0 milliliters of the filtered aliquot into a 25-milliliter volumetric flask and dilute to volume with the mobile phase described in § 452.60(b)(1)(i) of this chapter. Pipet 4.0 milliliters of this solution into another 25-milliliter volumetric flask and bring to volume with the mobile phase. The solution is stable at room temperature for 24 hours.

(*c*) *Calculations.* Determine the percent of azithromycin dissolved as follows:

$$\text{Percent azithromycin dissolved} = \frac{A_U \times P_s \times D_F \times 100}{A_s \times W_u}$$

where:

A_U = Area of the azithromycin peak (at a retention time equal to that observed for the standard) in the chromatogram of the sample;

A_S = Area of the azithromycin peak in the chromatogram of the azithromycin standard;

P_S = Azithromycin activity in the azithromycin working standard solution in micrograms per milliliter;

$$DF = \text{Dilution factor} = \frac{900^{1} \times 25 \times 25}{2 \times 4}$$

[1] If more than 15 milliliters of dissolution medium are removed, correct for the volume removed; and

W_U = Theoretical azithromycin content (mg) of capsule.

(15) *Cefprozil.* Proceed as directed in § 442.80(b)(1) of this chapter except:

(i) *Sample solutions.* Filter the sample solutions through a 0.45-micron filter before use. Use the sample solution as it is removed from the dissolution vessel without further dilution for the 250-milligram tablet; prepare the sample solution for the 500-milligram tablet by diluting a 5-milliliter aliquot of the filtered solution to volume in a 10-milliliter volumetric flask with distilled water.

(ii) *Calculations.* Determine the total percent of cefprozil dissolved as follows:

$$\text{Total percentage dissolved} = \frac{(\text{mg cefprozil (Z) dissolved} + \text{mg cefprozil (E) dissolved})}{\text{label claim}}$$

$$\text{Milligrams of cefprozil (Z) or cefprozil (E) dissolved} = \frac{A_U \times c \times d \times 900}{A_s}$$

where:
A_U = Area of the cefprozil (Z) or cefprozil (E) response in the chromatogram of the sample (at a retention time equal to that observed for the standard);
A_S = Area of the cefprozil (Z) or cefprozil (E) response in the chromatogram of the cefprozil (Z) or cefprozil (E) standard;
c = Concentration of the cefprozil (Z) or cefprozil (E) working standard solution in milligrams per milliliter; and
d = Dilution factor of the sample filtrate.

(16) *Loracarbef*—(i) *Preparation of the working standard solution.* Accurately weigh approximately 110 milligrams of the loracarbef working standard into a suitable-sized volumetric flask. Dissolve and dilute to volume with water. Further dilute an accurately measured portion with distilled water to obtain a known concentration of 0.02 milligram of loracarbef activity per milliliter.

(ii) *Preparation of sample solutions.* Dilute an accurately measured portion of the sample with sufficient distilled water to obtain a concentration of 0.02 milligram of loracarbef activity per milliliter (estimated).

(iii) *Procedure.* Using a suitable spectrophotometer and water as the blank, determine the absorbance of each standard and sample solution at the absorbance maximum at approximately 260 nanometers. Determine the exact position of the absorbance maximum for the particular instrument used.

(iv) *Calculations.* Determine the total amount of loracarbef dissolved as follows:

$$T = \frac{A_U \times c \times d \times 900}{A_s}$$

where:
T = Total milligrams of loracarbef activity dissolved;
A_U = Absorbance of sample;
A_S = Absorbance of the standard;
c = Concentration of the working standard solution in milligrams per milliliter; and
d = Dilution factor of the sample filtrate.

(17) *Cefadroxil hemihydrate.* Proceed as directed in paragraph (c)(1) of this section, except use the cefadroxil working standard and measure the absorbance at the absorption peak of approximately 264 nanometers.

(18) *Rifabutin*—(i) *Preparation of the working standard solution.* Accurately weigh approximately 45 milligrams of the rifabutin working standard into a suitable-sized volumetric flask. Dissolve and dilute to volume with 0.01*N* hydrochloric acid (prepared by diluting 5.0 milliliters of hydrochloric acid (37 percent) to 6 liters with distilled water) to obtain a concentration of approximately 13 micrograms rifabutin activity per milliliter.

(ii) *Preparation of sample solutions.* Forty-five minutes after the beginning of the rotation, withdraw a 10-milliliter aliquot from the vessel. Dilute a 2-milliliter portion of the sample to 25 milliliters with 0.01*N* hydrochloric acid.

(iii) *Procedure.* Using a suitable spectrophotometer and 0.01*N* hydrochloric acid as the blank, determine the absorbance of each standard and sample solution at the absorbance maximum at approximately 280 nanometers. Determine the exact position of the absorbance maximum for the particular instrument used.

(iv) *Calculations.* Determine the total amount of rifabutin dissolved as follows:

$$T = \frac{A_U \times c \times d \times 900}{A_s \times 1{,}000}$$

where:
T = Total milligrams of rifabutin activity dissolved;
A_U = Absorbance of sample;
A_S = Absorbance of the standard;
c = Rifabutin activity of the working standard solution in micrograms per milliliter; and
d = Dilution factor of the sample filtrate.

(19) *Cefpodoxime proxetil*—(i) *Dissolution fluid: 0.04 molar glycine buffer, pH 3.0*—(A) *Stock solution.* Dissolve 54.5 grams of glycine (aminoacetic acid) and 42.6 grams of sodium chloride in about 500 milliliters of deionized water in a 1-liter volumetric flask. Add cautiously, and with swirling, 14.2 milliliters of concentrated hydrochloric acid. Cool to room temperature. Dilute to volume with deionized water and mix. Check the pH of the solution obtained by diluting 50 milliliters of the stock solution to 900 milliliters with deionized water. The pH should be 3.0±0.1. If necessary, adjust the pH of the stock solution with 50 percent sodium hydroxide or concentrated hydrochloric acid. Recheck that the pH of the working solution is 3.0±0.1.

(B) *Working solution.* Dilute 50 milliliters of stock solution to 900 milliliters with deionized water.

(ii) *Preparation of the working standard solutions.* Accurately weigh approximately 28 milligrams for the 100-milligram tablets and 56 milligrams for the 200-milligram tablets of the cefpodoxime proxetil working standard and dissolve in 10 milliliters of methanol. Dilute to 200 milliliters with dissolution fluid. Prepare fresh daily.

(iii) *Sample solutions.* Filter the sample solutions through a 0.45-micron filter before use. Use the sample solution as it is removed from the dissolution vessel without further dilution.

(iv) *Procedure.* Using a suitable spectrophotometer and water as the blank, determine the absorbance of each standard and sample solution at the absorbance peak at approximately 259 nanometers. Determine the exact position of the absorption peak for the particular instrument used.

(v) *Calculations.* Determine the percent of label dissolved as follows:

$$\text{Percent dissolved} = (A_{sam}/A_{std}) \times (C_s/L) \times V \times P \times F1$$

where:

A_{sam} = Absorbance of the sample at 259 nanometers;

A_{std} = Absorbance of the working standard solution at 259 nanometers;

C_s = Concentration of the working standard preparation in milligrams per milliliter;

L = Tablet strength, in milligrams per tablet;

P = Purity of the reference standard in percent;

V = Volume of dissolution fluid used in milliliters (900); and

$F1$ = 0.7666 (conversion factor to free acid equivalents).

(d) *Evaluation.* Use the dissolution acceptance table and interpretation in the United States Pharmacopeia XXI.

[44 FR 48188, Aug. 17, 1979]

EDITORIAL NOTE: For FEDERAL REGISTER citations affecting § 430.215, see the List of CFR Sections Affected appearing in the Finding Aids section of this volume.

§ 436.216 High-performance liquid chromatographic assay.

(a) *Equipment.* A suitable high-performance liquid chromatograph equipped with:

(1) A suitable detection system specified in the monograph for the drug being tested;

(2) A suitable recording device of at least 25-centimeter deflection;

(3) A suitable chromatographic data managing system; and

(4) An analytical column, 3 to 30 centimeters long, packed with a material as defined in the monograph for the drug being tested; and if specified in that monograph, the inlet of this column may be connected to a guard column, 3 to 5 centimeters in length, packed with the same material of 40 to 60 micrometers particle size.

(b) *Procedure.* Perform the assay and calculate the drug content using the temperature, instrumental conditions, flow rate, and calculations specified in the monograph for the drug being tested. Use a detector sensitivity setting that gives a peak height for the working standard solution that is at least 50 percent of scale with typical chart speed of not less than 2.5 millimeters per minute. Use the equipment described in paragraph (a) of this section. Use the reagents, working standard solution, and sample solution described in the monograph for the drug being tested. Equilibrate and condition the column by passage of 10 to 15 void volumes of mobile phase followed by five replicate injections of the same volume of the working standard solution. Allow an operating time sufficiently long to obtain satisfactory separation and elution of the expected components after each injection. Record the peak responses and calculate the prescribed